ACKNOWLEDGEMENT

These studies were financed by the Italian MAP and the Commission of EU (Contract FAIR CT 95-0260).

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An Umpolung approach to fluorinated non-ester pyrethroids

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Abstract: The synthesis of novel, fluorinated non-ester pyrethroids by electrophilic fluorination of a stabilised anion with *N*-fluorobenzenesulfonimide is reported.

Keywords: non-ester pyrethroids; electrophilic fluorination

1 INTRODUCTION

The introduction of fluorine into biologically active compounds is of interest as it alters the metabolism, stereoelectronics and lipophilicity of the molecule, yet is isosteric to the proton equivalent. In the case of pyrethroid insecticides, introduction of fluorine also alters the spectrum of activity.[1] However, no information is available on the effect of fluorination at the benzylic position of the central region. The nature of the substituents at this position is known to alter the activity of pyrethroids, especially towards resistant strains of insects.

2 EXPERIEMENTAL

The fluorine anion is a poor nucleophile and often requires special reagents for its introduction, such as diethylaminosulfur trifluoride (DAST), which participates in the reaction by supplying the fluorine atom and creating an excellent leaving group. The generation of this leaving group prevents the use of DAST in the synthesis of non-ester pyrethroids because undesirable alkene or cyclopropane rearrangement[2] and *ipso* reaction of the aromatic groups may all occur under these conditions. In contrast, a cyano group at the benzylic position, known to enhance insecticidal activity in many pyrethroids, can stabilise a negative charge thus allowing fluorine to be introduced regioselectively under *electrophilic* conditions. Of the several reagents available for this transformation we chose *N*-fluorobenzenesulfonimide.

Alkenes **1a–f** (Fig 1) and alkanes **3a,b,f** (Fig 1) are either known compounds or analogues of known compounds and were prepared by literature procedures. Deprotonation of alkenes **1a–e** was achieved by lithium bis(trimethylsilyl)amide to produce a delocalised anion with negative charge expected to be stabilised *alpha* to the cyano group. Introduction of the fluorine electrophile yielded only one detectable regioisomer (**2a–e**) with concomitant deconjugation to generate an (*E*)-olefin. The fluorination reaction was also performed successfully on compounds

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Contract/grant sponsor: British Technology Group plc.
Contract/grant sponsor: Biotechnology and Biological Sciences Research Council.
(*Received 3 July 1998; accepted 16 December 1998*)

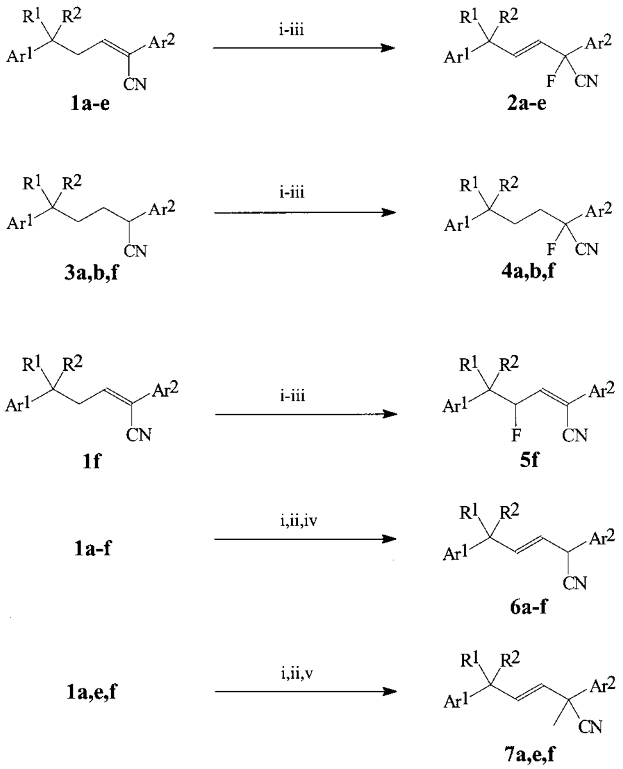

Figure 1(a). The regioselectivity of electrophilic fluorination compared with methylation and acidic quench of the anion. (i) LiHMDS, −78°C to 0°C, 1 h; (ii) −78°C; (iii) $(PhSO_2)_2NF$; (iv) 2 M HCl; (v) excess MeI.

3a,b,f, to yield the expected products **4a,b,f**. Yields for the reaction varied from 40 to 90% and no diastereoselectivity was observed for the products **2a–d**. Regioselective control of fluorination *alpha* to the cyano group was complete except in the reaction of **1f**. In this case fluorination yielded **5f**, the opposite regioisomer to that expected and although the yield was moderate (33%) this was the only regioisomer detected. Varying reaction conditions did not produce the desired regioisomer. To examine whether this change in regioselectivity was determined before addition of the electrophile, the anion of **1f** was quenched with 2 M hydrochloric acid and iodomethane. The products, **6f** and **7f** respectively, showed the same regioselectivity observed for **6a–e**, **7a** and **7e**, so it is only the reaction of **1f** with the fluorinating agent that generates unexpected regiochemistry. The difference in reactivity of the anion of **1f** compared with **1a–e** is unlikely to be based upon steric grounds, as **1a–d** are less hindered and **1e** more hindered, nor is it due to hyperconjugation. The explanation may involve delivery of the fluorine by an interaction of the cyclopropane ring with the fluorinating reagent but this hypothesis has not been tested.

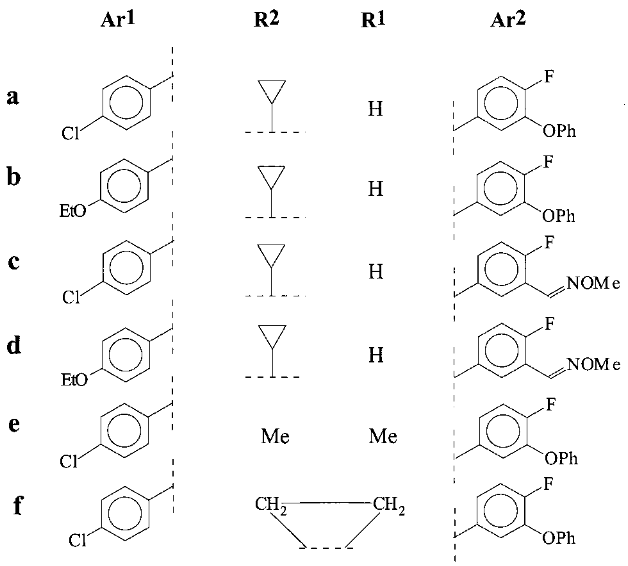

Figure 1(b). Substituents in the analogues depicted in Fig. 1(a).

Results of bioassay of these compounds will be reported elsewhere.

ACKNOWLEDGEMENTS

The study received financial support from the British Technology Group plc. IACR-Rothamsted receives grant-aided support from the Biotechnology and Biological Sciences Research Council.

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Resistance to glyphosate in *Lolium rigidum*

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Abstract: Annual ryegrass (*Lolium rigidum*) is a widespread and important weed of Australia and populations of this weed have developed resistance to most major herbicides, including glyphosate. The possible mechanisms of resistance have been examined in one glyphosate-resistant *Lolium* population. No major differences were observed between resistant and susceptible biotypes in respect of (i) the target enzyme (EPSP synthase), (ii) DAHP synthase, the first enzyme of the target (shikimate) pathway, (iii) absorption of glyphosate, or (iv) translocation. Following treatment with glyphosate, there was greater accumulation of shikimate (derived from shikimate-3-Pi) in susceptible than in resistant plants. In addition, the resistant population exhibited cross-resistance to 2-hydroxy-3-(1,2,4-triazol-1-yl)propyl phosphonate, a herbicide which, although structurally similar to glyphosate, acts at an unrelated target site. On the basis of these observations we speculate that movement of glypho-